

In the Claims

Amended Claims 1 through 8 are as follows, and appear in an *unmarked* claim listing in Appendix C.

1. (Currently amended, having been twice previously amended) A surgically modified nonhuman mammalian animal model comprising an nonhuman mammalian animal having a preoperative weight, a preoperative endogenous ghrelin production and a preoperative substantially normal animal gastrointestinal system tract that has been surgically modified undergone a surgical modification, wherein said surgical modification reduces the volume of the a stomach of said gastrointestinal tract leaving a residual gastric pouch that food enters and in which food is lodged while undergoing digestion, and reduces the digestive area of said gastrointestinal tract; and, wherein postoperatively, said surgically modified nonhuman mammalian animal exhibits a substantially permanent reduction of said preoperative weight and a substantially permanent reduction in said preoperative endogenous ghrelin production.

2. (Previously amended) The nonhuman mammalian animal model of claim 1, wherein said nonhuman mammalian animal is selected for the surgical modification from the group comprising murine, ovine, porcine, caprine, canine, feline, and primate nonhuman mammalian animals.

3. (Currently cancelled, having been twice previously amended) The nonhuman mammalian animal model of claim 1, wherein said nonhuman mammalian animal is selected for the surgical

modification from the group comprising already existing transgenic murine, ovine, porcine, caprine, canine, feline, and primate nonhuman mammalian animals.

4. (Once Amended) The nonhuman mammalian animal model of claim 1 wherein said animal is a Zucker rat.

5. (Currently amended, having been twice previously amended) The nonhuman mammalian animal model of claim of claim 1, wherein said nonhuman mammalian animal is selected for the surgical modification from the group comprising already existing genetically modified murine, ovine, porcine, caprine, canine, feline, and nonhuman mammalian animals that express an obese phenotype.

6. (Currently cancelled, having been twice previously amended) The nonhuman mammalian animal model of claim 1, wherein said nonhuman mammalian animal is selected for the surgical modification from the group comprising already existing cloned murine, ovine, porcine, caprine, canine, feline, and nonhuman mammalian animals.

7. (Currently amended having been once previously amended) The nonhuman mammalian animal model of claim 1, wherein said surgical modification is selected from the group comprising bariatric surgeries that leave a gastric pouch that food enters and in which food is lodged while undergoing digestion, biliopancreatic diversion that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastric banding that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion,

a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastric reduction that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastric by-pass that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastrectomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastrocolostomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastroduodenostomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastroenterocolostomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastroenteroplasty that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastroenterostomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastroenterotomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastroesophagostomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastrogastrostomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastroileostomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastrojejunostomy that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, gastroplasty that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, vertical banded gastroplasty that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, intestinal bypass that leaves a gastric pouch that food enters and in which food is lodged while undergoing digestion, restriction operations that

leave a gastric pouch that food enters and in which food is lodged while undergoing digestion,
and weight-loss surgerythat leave a gastric pouch that food enters and in which food is lodged
while undergoing digestion.

8. (Once Amended) The nonhuman mammalian animal model of claim 4 wherein said Zucker rat has undergone a Roux-en-Y gastroplasty.

9. (Withdrawn and currently cancelled) A method for performing a Roux-en-Y gastroplasty on a Zucker Rat comprising the steps of:

- a. administering anesthesia;
- b. shaving and sterilizing the abdomen of said Zucker rat;
- c. incising the abdomen of said Zucker rat;
- d. identifying the terminal esophagus, lesser curvature of the stomach, and greater curvature of the stomach of said Zucker rat;
- e. dissecting the terminal esophagus, lesser curvature of the stomach, and greater curvature of the stomach of said Zucker rat free of their surrounding supportive and membranous tissues;
- f. creating a gastric pouch having a volume of about 20% of the presurgical stomach of said Zucker

rat;

g. dividing the jejunum of said Zucker rat at a location about 16 cm below the ligament of Treitz, thereby creating a distal portion of the divided jejunum and a proximal portion of the divided jejunum of said Zucker rat;

h. performing a gastrojejunostomy on said Zucker rat by anastomosing the distal portion of the divided jejunum of said Zucker rat to a site on the anterior surface of the gastric fundus of said Zucker rat;

i. performing a jejunojejunostomy on said Zucker rat by anastomosing the proximal aspect of the divided jejenum of said Zucker rat to a site at a distance of about 10 cm below the site of the gastrojejunostomy;

j. closing the stump of the proximal portion of the divided jejunum of said Zucker rat;

k. closing the incised abdomen of said Zucker rat.

10. (Withdrawn and presently cancelled) The method of claim 9, wherein said step of creating a gastric pouch further comprises the steps of:

a. placing a first row of surgical staples across the stomach of said Zucker rat about 2-3 mm

- below the gastroesophageal junction of said Zucker rat;
- b. placing a second row of surgical staples across the stomach of said Zucker rat about 4–5 mm below the gastroesophageal junction of said Zucker rat;
- c. reinforcing said first and second row of surgical staples with sutures.

11. (Withdrawn and presently cancelled) A method for investigating the biological mechanisms of obesity and reducing obesity comprising the steps of:

- a. selecting a plurality of animals for confinement in a common controlled laboratory environment;
- b. dividing said plurality of animals into at least three groups, wherein each member of a first group of said plurality of animals undergoes a sham operation and is thereafter permitted to consume amounts of liquid nutrients and solid nutrients ad libitum; and, wherein each member of a second group of said plurality of animals undergoes a surgical modification of its gastrointestinal tract and is thereafter permitted to consume amounts of liquid nutrients and solid nutrients ad libitum; and, wherein each member of a third group of said plurality of animals undergoes said sham operation and is thereafter permitted to feed only a mean of said amounts of liquid nutrients and solid nutrients consumed by said members of said second group of said plurality of animals;

- c. daily measuring and recording a preoperative number of calories consumed per meal, a preoperative number of grams of nutrients consumed per meal, and a preoperative number of meals taken by each member of each of said first, second and third groups of said plurality of animals;
- d. daily measuring and recording a preoperative body weight of each member of each of said first, second and third groups of said plurality of animals;
- e. daily calculating and recording a preoperative total daily caloric intake and a preoperative total daily number of grams of nutrients consumed by each member of each of said first, second and third groups of said plurality of animals;
- f. performing said surgical modification of said gastrointestinal tract of each of said members of said second group of said plurality of animals;
- g. permitting each of said members of said second group of said plurality of animals to resume eating and drinking about 24 hours postoperatively;
- h. performing said sham operation on each of said members of said first and second groups of said plurality of animals;
- i. permitting each of said members of said first and second groups of said plurality of animals to

resume eating and drinking about 24 hours postoperatively;

j. feeding each member of said first and second groups of said plurality of animals a diet of liquid nutrients ad libitum for about 4 postoperative days.

k. additionally feeding each member of said first and second groups of said plurality of animals solid nutrients ad libitum on about a 5th postoperative day and continuing until a sacrifice of said members of said first and second groups.

l. feeding each member of said third group of said plurality of animals a diet of liquid nutrients in an amount equal to a mean amount of liquid nutrients consumed by said members of said second group for said about 4 postoperative days.

m. additionally feeding said members of said third group of said plurality of animals an amount equal to a mean amount of solid nutrients consumed by said members of said second group of said plurality of animals, beginning on about a 5th postoperative day and continuing until a sacrifice of said members of said third group.

n. daily measuring and recording a postoperative number of calories consumed per meal, a postoperative number of grams of nutrients consumed per meal, and a postoperative number of meals taken by each member of each of said first, second and third groups of said plurality of animals;

- o. daily measuring and recording a postoperative body weight of each member of each of said first, second and third groups of said plurality of animals;
- p. daily calculating and recording a postoperative total daily caloric intake and a postoperative total daily number of grams of nutrients consumed by each member of each of said first, second and third groups of said plurality of animals;
- q. daily calculating and recording a postoperative number of calories consumed per meal, a postoperative number grams of nutrients consumed per meal and a postoperative number of meals taken by each member of each of said first, second and third groups of said plurality of animals;
- r. sacrificing said plurality of animals on a common postoperative day;
- s. postmortem, comparing said preoperative and said postoperative total daily caloric intake, said preoperative and said postoperative total daily number of grams of nutrients consumed, said preoperative and said postoperative number of calories consumed per meal, said preoperative and said postoperative number of grams of nutrients consumed per meal, said preoperative and said postoperative number of meals taken, and said preoperative and said postoperative body weight for each member of said first, second and third groups of said plurality of animals;

t. postmortem, measuring and comparing biological factors relating to biological mechanisms of obesity and reduction of obesity.

12. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of selecting a plurality of animals for confinement in a common controlled laboratory environment further comprises selecting a plurality of animals having substantially comparable ages and preoperative body weights.

13. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of selecting a plurality of animals for confinement in a common controlled laboratory environment further comprises selecting said plurality of animals from the group comprising murine, ovine, porcine, caprine, canine, feline, and primate animals.

14. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of selecting a plurality of animals for confinement in a common controlled laboratory environment further comprises selecting said plurality of animals from the group comprising transgenic murine, ovine, porcine, caprine, canine, feline, and primate animals.

15. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of selecting a plurality of animals for confinement in a common controlled laboratory environment further comprises selecting said plurality of animals from the group comprising genetically modified

murine, ovine, porcine, caprine, canine, feline, and primate animals.

16. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of selecting a plurality of animals for confinement in a common controlled laboratory environment further comprises selecting said plurality of animals from Zucker rats.

17. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of selecting a plurality of animals for confinement in a common controlled laboratory environment further comprises selecting said plurality of animals from the group comprising cloned murine, ovine, porcine, caprine, canine, feline, and primate animals.

18. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of performing said surgical modification of said gastrointestinal tract of each of said members of said second group of said plurality of animals further comprises selecting said surgical modification from the group comprising bariatric surgeries, biliopancreatic diversion, gastric banding, gastric reduction, gastric by-pass, gastrectomy, gastrocolostomy, gastroduodenostomy, gastroenterocolostomy, gastroenteroplasty, gastroenterostomy, gastroenterotomy, gastroesophagostomy, gastrogastrostomy, gastroileostomy, gastrojejunostomy, gastroplasty, vertical banded gastroplasty, intestinal bypass, restriction operations, and weight-loss surgery.

19. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of dividing said plurality of animals into at least three groups further comprises selecting said second group

of animals from Zucker rats and surgically modifying said gastrointestinal tract of each of said members of said second group by means of a Roux-en-Y gastroplasty.

20. (Withdrawn and presently cancelled) The method of claim 11, wherein said sham operation comprises opening and closing the abdomen of said members of said first and third groups of said plurality of animals.

21. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of selecting a plurality of animals for confinement in a common controlled laboratory environment further comprises confining said plurality of animals to a common cage having a common standardized source of food and water for a period of about one week after their selection to acclimatize them to their surroundings.

22. (Withdrawn and presently cancelled) The method of claim 11, wherein said step of selecting a plurality of animals for confinement in a common controlled laboratory environment further comprises providing said controlled environment with an ambient temperature of about 26°C, a relative humidity of about 45%, and a 12-hour light/dark cycle.

23. (Withdrawn and presently cancelled) The method of claim 11, wherein said step dividing said plurality of animals into at least three groups further comprises, initially confining each member of said plurality of animals to an individual cage for a period of about 1 week, equipped with a device to continuously feed, measure, calculate and record said preoperative total daily

number of grams of nutrients consumed, said preoperative number of calories consumed per meal, said preoperative number of grams of nutrients consumed per meal, said preoperative number of meals taken, and said preoperative body weight for each member of said first, second and third groups of said plurality of animals.